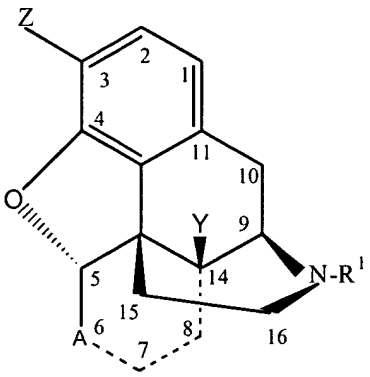
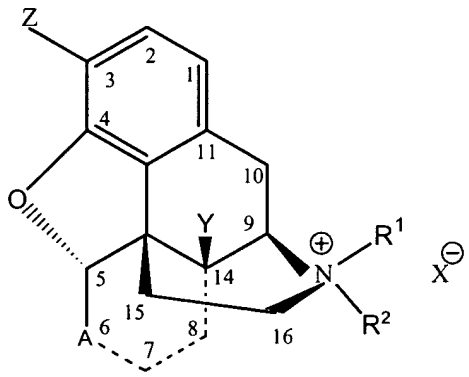
AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A process for the preparation of a quaternary derivative of a tertiary N-substituted morphinan alkaloid, the process comprising contacting a tertiary N-substituted morphinan alkaloid substrate with an alkylating agent in an anhydrous solvent system, wherein the solvent system comprises an aprotic dipolar solvent **selected from the group consisting of dimethylacetamide, dimethylformamide, 1-methyl-2-pyrrolidinone, hexamethylphosphoramide, and mixtures thereof** with the aprotic dipolar solvent constituting at least 25 wt % of the solvent system, **the contacting is carried out within a temperature range of about 55°C to about 85°C,** the tertiary N-substituted morphinan alkaloid substrate ~~has the structure of Formula 1~~ and the quaternary derivative ~~has the structure of Formula 1A:~~ **correspond to Formulae 1 and 1A, respectively:**



Formula 1



Formula 1A

~~wherein~~

A is -C(O)-, -C(S)-, -C(=CH_2)-, **[[**-CHA_1- or -CA_1=**]]** **-CH(A_1)-, or -C(A_1)=**,

A_1 is hydroxy, alkoxy, or acyloxy,

each R is independently hydrocarbyl,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

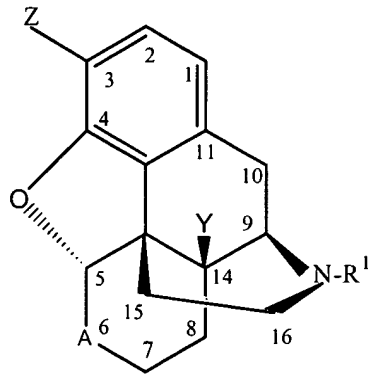
$X^{\ominus}$is an anion,

Y, if present, is hydrogen, hydroxy, alkoxy, **[[**or**]]** acyloxy, **-OTHP, -OSiR$_3$, -OBn, -OBs, -OTs, or -OMs,**

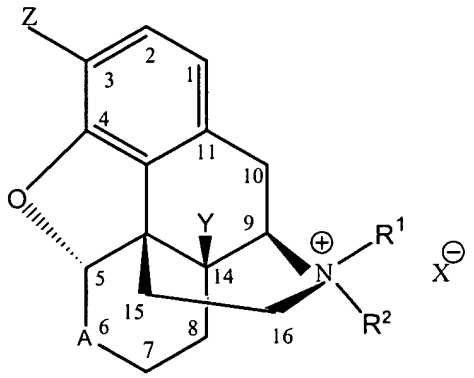
Z is hydroxy, alkoxy, **[[**or**]]** acyloxy, **-OTHP, -OSiR$_3$, -OBn, -OBs, -OTs, or -OMs,** and

the dashed lines between the carbon atoms at positions 6 and 7, 7 and 8, and 8 and 14, respectively, represent (i) carbon-carbon single bonds, (ii) carbon-carbon single bonds between positions 6 and 7 and between positions 8 and 14, and a double bond between positions 7 and 8, or (iii) conjugated carbon-carbon double bonds between positions 6 and 7 and positions 8 and 14, with the proviso that Y is not present if there is a double bond between the carbons at positions 8 and 14.

2. (Currently amended) The process of claim 1 wherein the tertiary **N-substituted** morphinan alkaloid substrate ~~is represented by Formula 2~~ and the quaternary derivative ~~is represented by Formula 2A.~~ **correspond to Formulae 2 and 2A, respectively:**



Formula 2



Formula 2A

~~wherein~~

A is -C(O)-, -C(S)-, -C(=CH$_2$)-, or **[[**-CHA$_1$-**]]** **-CH(A$_1$)-**,

A$_1$ is hydroxy, alkoxy, or acyloxy,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl, **[[**and**]]**

$X^{\ominus}$ is an anion,

Y**[[**,**]]** is hydrogen, hydroxy, alkoxy, or acyloxy, and

Z is hydroxy, alkoxy, or acyloxy.

3. (Currently amended) The process of claim 2 wherein the tertiary **N-substituted** morphinan alkaloid substrate is naltrexone ((5α)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-one), oxymorphone ((5α)-4,5-epoxy-3,14-dihydroxy-17-methylmorphinan-6-one), oxycodone ((5α)-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one), hydromorphone ((5α)-4,5-epoxy-3-hydroxy-17-methylmorphinan-6-one), naloxone ((5α)-4,5-epoxy-3,14-dihydroxy-17-(2-propenyl)morphinan-6-one), nalmefene ((5α)-17-(cyclopropylmethyl)-4,5-epoxy-6-methylenemorphinan-3,14-diol) or nalbuphine ((5α)-17-(cyclobutylmethyl)-4,5-epoxymorphinan-3,6,14-triol).

4-5. (Canceled)

6. (Presently pending) The process of claim 1 wherein the alkylating agent is methyl bromide.

7. (Presently pending) The process according to claim 1 wherein said process is carried out at a pressure of less than 1.25 atmospheres.

8-10. (Canceled)

11. (Presently pending) The process according to claim 1 wherein the aprotic dipolar solvent constitutes at least 75 wt. % of the solvent system.

12-14. (Canceled)

15. (Presently pending) The process according to claim 1 wherein said aprotic dipolar solvent is 1-methyl-2-pyrrolidinone.

16-27. (Canceled)

28. (Presently pending) The process according to claim 1 wherein Y and Z are independently $-OCH_3$, -OAc, -OTHP, $-OSiR_3$, -OBn, -OBz, -OBs, -OTs, or -OMs wherein each R is independently hydrocarbyl.

29. (Presently pending) The process according to claim 1 wherein said anhydrous solvent system contains less than 0.2 wt. % water and is maintained in a moisture-free atmosphere in a reaction vessel.

30. (Presently pending) The process according to claim 1 wherein said anhydrous solvent system contains less than 0.1 wt. % water.

31. (Presently pending) The process according to claim 1 wherein said anhydrous solvent system contains less than 0.05 wt. % water.

32. (Presently pending) The process according to claim 31 wherein said alkylating agent is a methylating agent.

33. (Canceled)

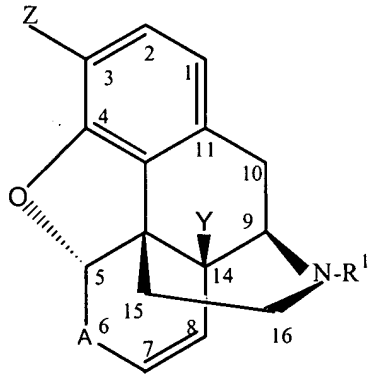
34. (Presently pending) The process according to claim 31 wherein said alkylating agent and said substrate are present in a mole ratio of between 1:1 and 1.5:1, respectively.

35. (Canceled)

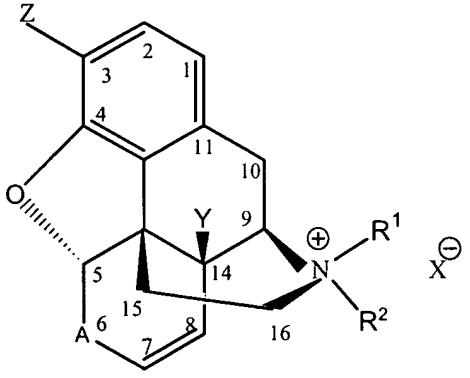
36. (Currently amended) The process according to claim 1 wherein said anhydrous ~~dipolar aprotic~~ solvent **system** and said substrate are present in a volume-to-weight ratio of 1.5:1 -1.75:1.

37. (Canceled)

38. (Currently amended) The process of claim 1 wherein the tertiary **N-substituted** morphinan alkaloid substrate ~~is represented by Formula 3~~ and the ~~product~~ **quaternary derivative** ~~is represented by Formula 3A.~~ **correspond to Formulae 3 and 3A, respectively:**



Formula 3



Formula 3A

~~wherein~~

A is -C(O)-, -C(S)-, -C(=CH_2)-, or **[[**-CHA_1-**]]** **-$CH(A_1)$-**,

A_1 is hydroxy, alkoxy, or acyloxy,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl, **[[and]]**

$X^{\ominus}$is an anion,

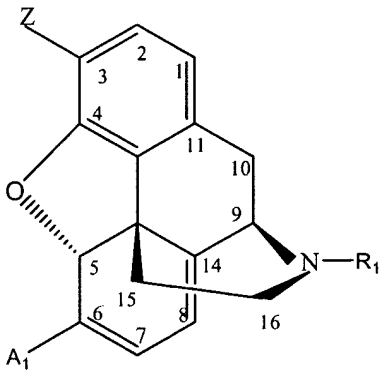
Y**[[,]]** is **[[H]]** **hydrogen**, hydroxy, alkoxy, or acyloxy, and

Z is hydroxy, alkoxy, or acyloxy.

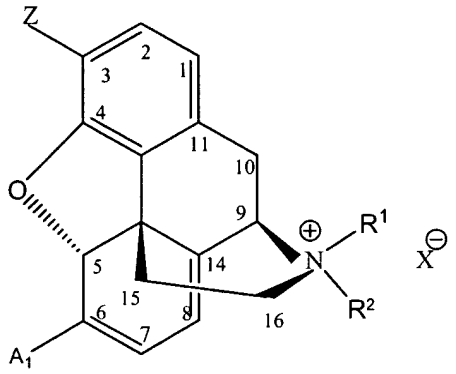
39. (Currently amended) The process of claim 38 wherein the tertiary **N-substituted** morphinan alkaloid substrate is morphine ((5α,6α)-7,8-didehydro-4,5-epoxi-17-methylmorphinan-3,6-diol), codeine ((5α,6α)-7,8-didehydro-4,5-epoxi-3-methoxy-17-methylmorphinan-6-ol), codeinone ((5α)-7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-one) or 14-hydroxy-codeinone ((5α)-7,8-didehydro-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one).

40-61. (Canceled)

62. (New) The process of claim 1 wherein the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative correspond to Formulae 4 and 4A, respectively:



Formula 4



Formula 4A

A_1 is hydroxy, alkoxy, or acyloxy,

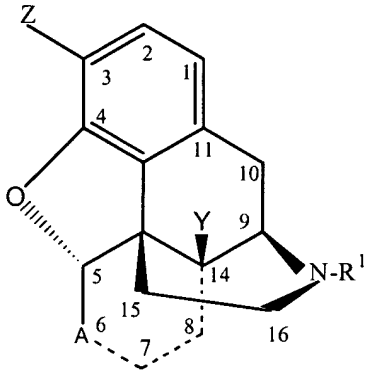
R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

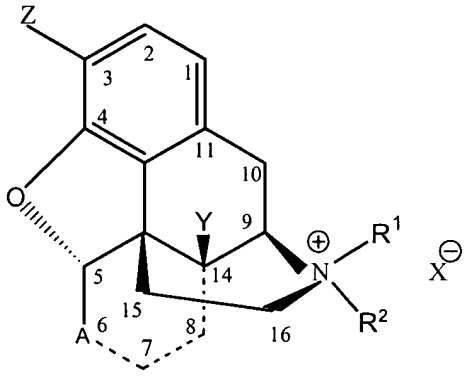
$X^{\ominus}$ is an anion, and

Z is hydroxy, alkoxy, or acyloxy.

63. (New) A process for the preparation of a quaternary derivative of a tertiary N-substituted morphinan alkaloid, the process comprising contacting a tertiary N-substituted morphinan alkaloid substrate with an alkylating agent in an anhydrous solvent system, wherein the solvent system comprises 1-methyl-2-pyrrolidinone with the 1-methyl-2-pyrrolidinone constituting at least 25 wt % of the solvent system, the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative correspond to Formulae 1 and 1A, respectively:



Formula 1



Formula 1A

A is -C(O)-, -C(S)-, -C(=CH_2)-, -CH(A_1)-, or -C(A_1)=,

A_1 is hydroxy, alkoxy, or acyloxy,

each R is independently hydrocarbyl,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

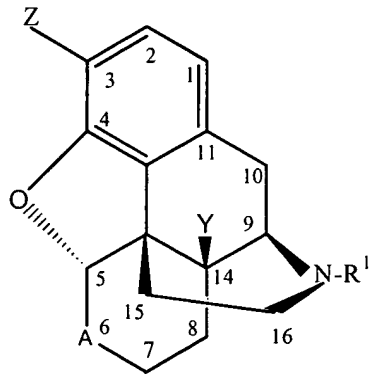
$X^{\ominus}$is an anion,

Y, if present, is hydrogen, hydroxy, alkoxy, acyloxy, -OTHP, -$OSiR_3$, -OBn, -OBs, -OTs, or -OMs,

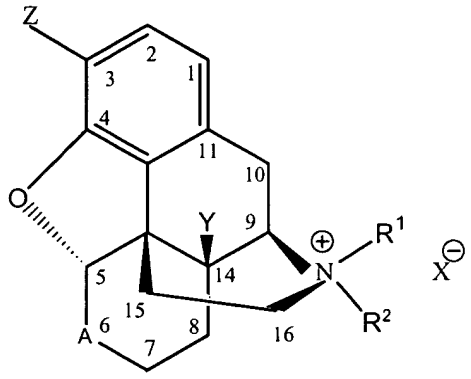
Z is hydroxy, alkoxy, acyloxy, -OTHP, -$OSiR_3$, -OBn, -OBs, -OTs, or -OMs, and

the dashed lines between the carbon atoms at positions 6 and 7, 7 and 8, and 8 and 14, respectively, represent (i) carbon-carbon single bonds, (ii) carbon-carbon single bonds between positions 6 and 7 and between positions 8 and 14, and a double bond between positions 7 and 8, or (iii) conjugated carbon-carbon double bonds between positions 6 and 7 and positions 8 and 14, with the proviso that Y is not present if there is a double bond between the carbons at positions 8 and 14.

64. (New) The process of claim 63 wherein the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative correspond to Formulae 2 and 2A, respectively:



Formula 2



Formula 2A

A is -C(O)-, -C(S)-, -$C(=CH_2)$-, or -$CH(A_1)$-,

A_1 is hydroxy, alkoxy, or acyloxy,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

$X^{\ominus}$is an anion,

Y is hydrogen, hydroxy, alkoxy, or acyloxy, and

Z is hydroxy, alkoxy, or acyloxy.

65. (New) The process of claim 64 wherein the tertiary N-substituted morphinan alkaloid substrate is naltrexone ((5α)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-one), oxymorphone ((5α)-4,5-epoxy-3,14-dihydroxy-17-methylmorphinan-6-one), oxycodone ((5α)-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one), hydromorphone ((5α)-4,5-epoxy-3-hydroxy-17-methylmorphinan-6-one), naloxone ((5α)-4,5-epoxy-3,14-dihydroxy-17-(2-propenyl)morphinan-6-one), nalmefene ((5α)-17-(cyclopropylmethyl)-4,5-epoxy-6-methylenemorphinan-3,14-diol) or nalbuphine ((5α)-17-(cyclobutylmethyl)-4,5-epoxymorphinan-3,6,14-triol).

66. (New) The process of claim 63 wherein the alkylating agent is methyl bromide.

67. (New) The process according to claim 63 wherein said process is carried out at a pressure of less than 1.25 atmospheres.

68. (New) The process according to claim 63 wherein the 1-methyl-2-pyrrolidinone constitutes at least 75 wt. % of the solvent system.

69. (New) The process according to claim 63 wherein Y and Z are independently $-OCH_3$, -OAc, -OTHP, $-OSiR_3$, -OBn, -OBz, -OBs, -OTs, or -OMs wherein each R is independently hydrocarbyl.

70. (New) The process according to claim 63 wherein said anhydrous solvent system contains less than 0.2 wt. % water and is maintained in a moisture-free atmosphere in a reaction vessel.

71. (New) The process according to claim 63 wherein said anhydrous solvent system contains less than 0.1 wt. % water.

72. (New) The process according to claim 63 wherein said anhydrous solvent system contains less than 0.05 wt. % water.

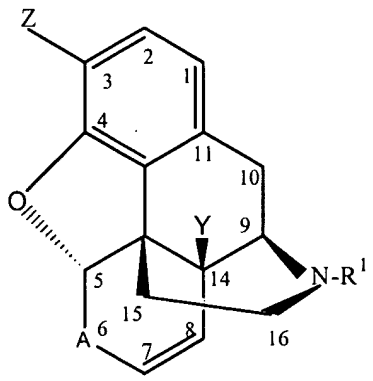
73. (New) The process according to claim 72 wherein said alkylating agent is a methylating agent.

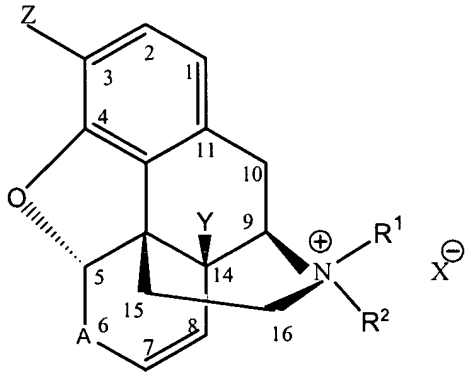
74. (New) The process according to claim 72 wherein said alkylating agent and said substrate are present in a mole ratio of between 1:1 and 1.5:1, respectively.

75. (New) The process according to claim 63 wherein said 1-methyl-2-pyrrolidinone and said substrate are present in a volume-to-weight ratio of 1.5:1-1.75:1.

76. (New) The process according to claim 63 wherein said contacting is carried out within a temperature range of about 55°C to about 85°C.

77. (New) The process of claim 63 wherein the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative correspond to Formulae 3 and 3A, respectively:





Formula 3 Formula 3A

A is -C(O)-, -C(S)-, -C(=CH_2)-, or -CH(A_1)-,

A_1 is hydroxy, alkoxy, or acyloxy,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

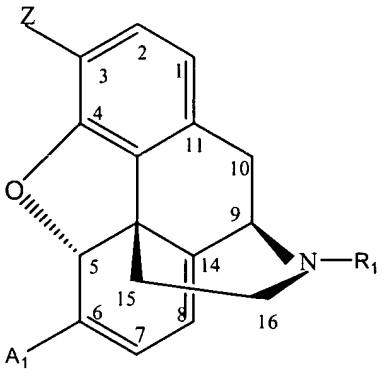
$X^{\ominus}$is an anion,

Y is hydrogen, hydroxy, alkoxy, or acyloxy, and

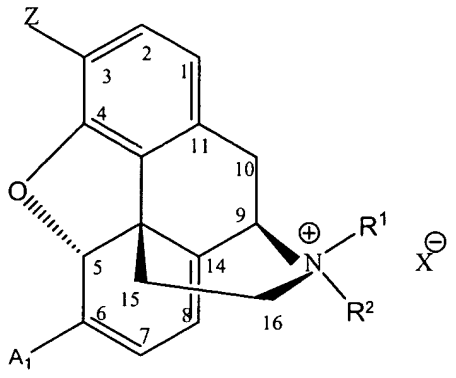
Z is hydroxy, alkoxy, or acyloxy.

78. (New) The process of claim 77 wherein the tertiary N-substituted morphinan alkaloid substrate is morphine ((5α,6α)-7,8-didehydro-4,5-epoxi-17-methylmorphinan-3,6-diol), codeine ((5α,6α)-7,8-didehydro-4,5-epoxi-3-methoxy-17-methylmorphinan-6-ol), codeinone ((5α)-7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-one) or 14-hydroxy-codeinone ((5α)-7,8-didehydro-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one).

79. (New) The process of claim 63 wherein the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative correspond to Formulae 4 and 4A, respectively:



Formula 4



Formula 4A

A_1 is hydroxy, alkoxy, or acyloxy,

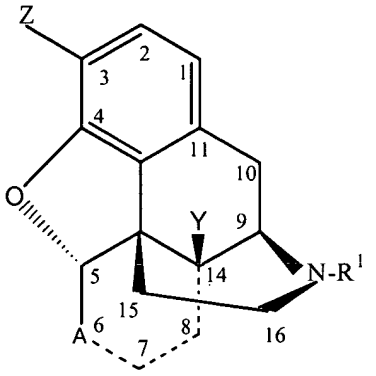
R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

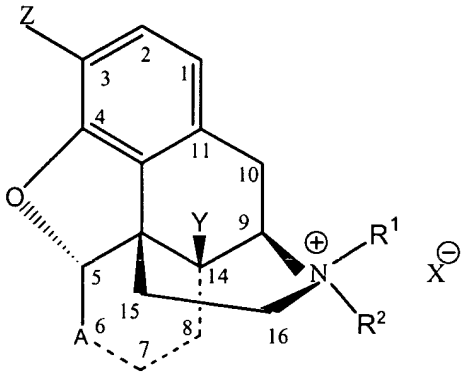
$X^{\ominus}$is an anion, and

Z is hydroxy, alkoxy, or acyloxy.

80. (New) A process for the preparation of a quaternary derivative of a tertiary N-substituted morphinan alkaloid, the process comprising contacting a tertiary N-substituted morphinan alkaloid substrate with methyl bromide in an anhydrous solvent system, wherein the solvent system comprises an aprotic dipolar solvent selected from the group consisting of dimethylacetamide, dimethylformamide, 1-methyl-2-pyrrolidinone, hexamethylphosphoramide, and mixtures thereof with the aprotic dipolar solvent constituting at least 25 wt % of the solvent system, the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative have the structures of Formulae 1 and 1A, respectively:



Formula 1



Formula 1A

A is -C(O)-, -C(S)-, -C(=CH_2)-, -CH(A_1)-, or -C(A_1)=,

A_1 is hydroxy, alkoxy, or acyloxy,

each R is independently hydrocarbyl,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

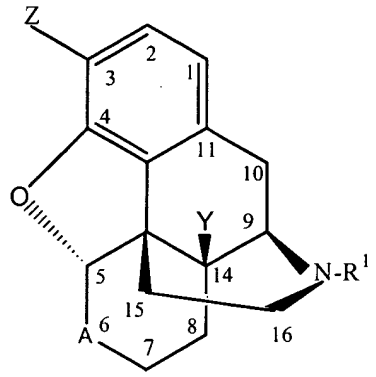
$X^{\ominus}$is an anion,

Y, if present, is hydrogen, hydroxy, alkoxy, acyloxy, -OTHP, -$OSiR_3$, -OBn, -OBs, -OTs, or -OMs,

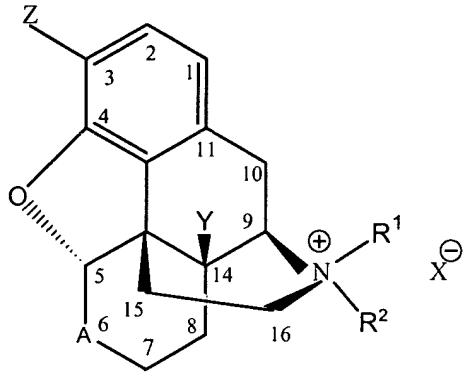
Z is hydroxy, alkoxy, acyloxy, -OTHP, -$OSiR_3$, -OBn, -OBs, -OTs, or -OMs, and

the dashed lines between the carbon atoms at positions 6 and 7, 7 and 8, and 8 and 14, respectively, represent (i) carbon-carbon single bonds, (ii) carbon-carbon single bonds between positions 6 and 7 and between positions 8 and 14, and a double bond between positions 7 and 8, or (iii) conjugated carbon-carbon double bonds between positions 6 and 7 and positions 8 and 14, with the proviso that Y is not present if there is a double bond between the carbons at positions 8 and 14.

81. (New) The process of claim 80 wherein the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative correspond to Formulae 2 and 2A, respectively:



Formula 2



Formula 2A

A is -C(O)-, -C(S)-, -C(=CH_2)-, or -CH(A_1)-,

A_1 is hydroxy, alkoxy, or acyloxy,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

$X^{\ominus}$is an anion,

Y is hydrogen, hydroxy, alkoxy, or acyloxy, and

Z is hydroxy, alkoxy, or acyloxy.

82. (New) The process of claim 81 wherein the tertiary N-substituted morphinan alkaloid substrate is naltrexone ((5α)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-one), oxymorphone ((5α)-4,5-epoxy-3,14-dihydroxy-17-methylmorphinan-6-one), oxycodone ((5α)-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one), hydromorphone ((5α)-4,5-epoxy-3-hydroxy-17-methylmorphinan-6-one), naloxone ((5α)-4,5-epoxy-3,14-dihydroxy-17-(2-propenyl)morphinan-6-one), nalmefene ((5α)-17-(cyclopropylmethyl)-4,5-epoxy-6-

methylenemorphinan-3,14-diol) or nalbuphine ((5α)-17-(cyclobutylmethyl)-4,5-epoxymorphinan-3,6,14-triol).

83. (New) The process according to claim 80 wherein said process is carried out at a pressure of less than 1.25 atmospheres.

84. (New) The process according to claim 80 wherein the aprotic dipolar solvent constitutes at least 75 wt. % of the solvent system.

85. (New) The process according to claim 80 wherein said aprotic dipolar solvent is 1-methyl-2-pyrrolidinone.

86. (New) The process according to claim 80 wherein Y and Z are independently $-OCH_3$, -OAc, -OTHP, $-OSiR_3$, -OBn, -OBz, -OBs, -OTs, or -OMs wherein each R is independently hydrocarbyl.

87. (New) The process according to claim 80 wherein said anhydrous solvent system contains less than 0.2 wt. % water and is maintained in a moisture-free atmosphere in a reaction vessel.

88. (New) The process according to claim 80 wherein said anhydrous solvent system contains less than 0.1 wt. % water.

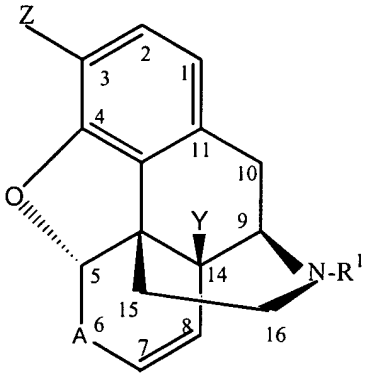
89. (New) The process according to claim 80 wherein said anhydrous solvent system contains less than 0.05 wt. % water.

90. (New) The process according to claim 89 wherein said methyl bromide and said substrate are present in a mole ratio of between 1:1 and 1.5:1, respectively.

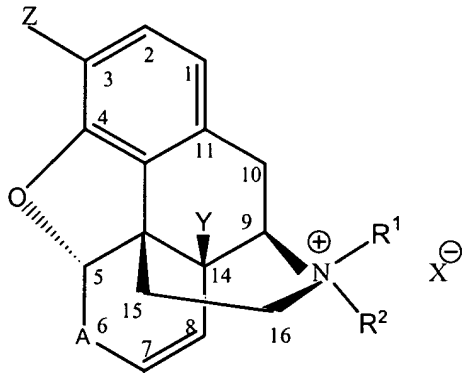
91. (New) The process according to claim 80 wherein said anhydrous solvent system and said substrate are present in a volume-to-weight ratio of 1.5:1-1.75:1.

92. (New) The process according to claim 80 wherein said contacting is carried out within a temperature range of about 55°C to about 85°C.

93. (New) The process of claim 80 wherein the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative correspond to Formulae 3 and 3A, respectively:



Formula 3



Formula 3A

A is -C(O)-, -C(S)-, -C(=CH_2)-, or -CH(A_1)-,

A_1 is hydroxy, alkoxy, or acyloxy,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

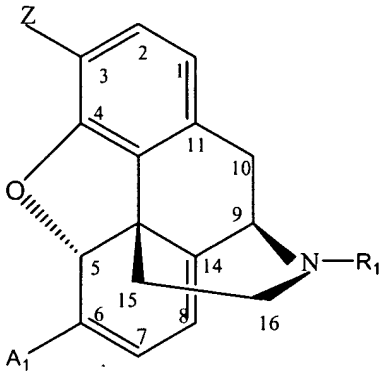
$X^{\ominus}$ is an anion,

Y is hydrogen, hydroxy, alkoxy, or acyloxy, and

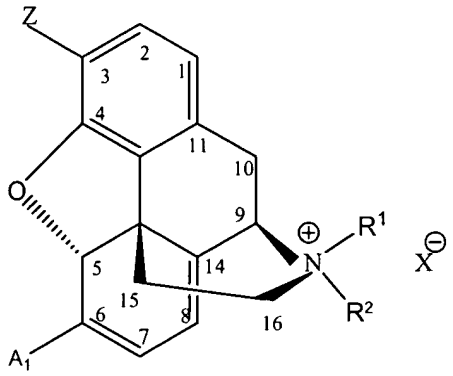
Z is hydroxy, alkoxy, or acyloxy.

94. (New) The process of claim 93 wherein the tertiary N-substituted morphinan alkaloid substrate is morphine ((5α,6α)-7,8-didehydro-4,5-epoxi-17-methylmorphinan-3,6-diol), codeine ((5α,6α)-7,8-didehydro-4,5-epoxi-3-methoxy-17-methylmorphinan-6-ol), codeinone ((5α)-7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-one) or 14-hydroxy-codeinone ((5α)-7,8-didehydro-4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one).

95. (New) The process of claim 80 wherein the tertiary N-substituted morphinan alkaloid substrate and the quaternary derivative correspond to Formulae 4 and 4A, respectively:



Formula 4



Formula 4A

A_1 is hydroxy, alkoxy, or acyloxy,

R^1 is hydrocarbyl or substituted hydrocarbyl,

R^2 is hydrocarbyl or substituted hydrocarbyl,

$X^{\ominus}$ is an anion, and

Z is hydroxy, alkoxy, or acyloxy.